PROGNOSTIC FACTORS FOR 6-YEAR SURVIVAL RATES OF PATIENTS WITH COPD

KOAH HASTALARININ 6 YILLIK SAĞKALIM ORANLARINI ETKİLEYEN PROGNOSTİK FAKTÖRLER

PROGNOSTIC FACTORS FOR PATIENTS WITH COPD

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Öz

Amaç: Kronik obstrüktif akciğer hastalığı (KOAH) dünyada morbidite ve mortalitenin önemli bir nedenidir. Bu çalışma, atak nedeniyle hastanemizde yatan KOAH' lı hastalarda 6 yıllık izlem verileri analiz ederek morbidite ve mortaliteyi etkileyen faktörleri belirlemek amacıyla yapılmıştır. Gereç ve Yöntem: Çalışmaya 2008 yılında yaşayan 64 ve ölen 114 hastanın 6 yıllık bilgileri kaydedildi. Bulgular: Gruplar arasında, sigara içme durumu (paket-yıl), majör komorbidite (koroner arter hastalığı, konjestif kalp yetmezliği, hipertansiyon ve diabetes mellitus) varlığı biomass, USOT kulanımı, non-invaziv mekanik ventilasyon ya da nebülizatör tedavisi, bazal hemoglobin, hematokrit, eritrosit sayımı, trombosit sayımı, erhythrocyte sedimantasyon hızı, CRP oranı, KOAH için kulanılan primer ilaçlar, biyokimyasal parametreler, arter kan gazı analizi bakımından fark tespit edilmedi. İkinci grupta % forced expiratory volum'ün 1.saniyesi (%FEV1) anlamlı düşüktü (p:0.038). Erkeklerde ortalam yaşam süresi 111.9±11.1 ay, bayanlarda 206.5±32.2 ay idi. Ortalama medyan survey erkeklerde 96, kadınlarda 180 ay idi. Tartışma: Bu çalışmada FEV1'in yaşayanlarda anlamlı yüksek olduğu ayrıca kadınların erkeklerden daha uzun yaşadığını tespit ettik.

Anahtar Kelimeler

Prognoz; Vucut Kitle İndeksi; Korpulmonale; Sürvey

Abstract

Aim: Chronic obstructive pulmonary disease (COPD) is an important cause of morbidity and mortality throughout the world. The objective of this study was to determine the factors influencing morbidity and mortality in patients hospitalized in a tertiary care center due to COPD exacerbation by analyzing the data of six-year follow-up. Meterial and Method: The enrolled patients were grouped as those who were alive by 2008 (n: 64) and those who were dead by 2008 (n: 114). Results: The groups did not differ in terms of smoking status, smoking burden (in pack-years), the presence of major comorbidities (namely coronary artery disease, congestive heart failure, hypertension and diabetes mellitus), the frequency of the patients with biomass exposure and the mean duration of exposure, the use of major drug classes prescribed for COPD, the rate of the use of LTOT, non-invasive mechanical ventilation or nebulisator, basal hemoglobin, hematocrite, white blood cell count, platelet count, erhythrocyte sedimentation rate, CRP levels, biochemical parameters, arterial blood gas analysis, and pulmonary function parameters other than average basal forced expiratory volume in 1 second (as percentage of predicted, which was lower in deceased group). The average lifetime with a diagnosis of COPD was 111.9±11.1 months for men and 206.5±32.2 months for women. Median survival time was 96 months in men and 180 months in women with COPD. Discussion: These results showed that FEV1 was significantly higher in people who live in, also found that women live longer than men

Keywords

Prognosis; Body Mass Index; Cor Pulmonale; Survey

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Introduction

Chronic obstructive pulmonary disease (COPD) is an inflammatory lung disease caused by noxious gases and particles and characterized by airflow obstruction that is not fully reversible. The disease is an important cause of morbidity and mortality throughout the world. COPD is the fourth leading cause of death in the world and is expected to rank third in 2020 [1].

The primary goals of COPD treatment are reduction of symptoms, prevention of exacerbations, lengthening of survival, and increase of quality of life. Although medical therapy including β2-agonists, anticholinergics, xanthine derivatives and corticosteroids is beneficial with regard to symptom control, effort capacity and quality of life, the sole treatment that provides a significant advantage of survival seems to be long-term oxygen treatment (LTOT) [2,3].

During the progressive course of the disease, the patients with COPD experience 1-4 exacerbations per year. Generally, the exacerbations result from infections; other reasons include heart failure, arrhythmias, pneumothorax, pulmonary embolism, inappropriate treatment, some medications suppressing respiration, some metabolic conditions, and malnutrition. Whatever the cause is, exacerbations increase the morbidity and mortality rates of COPD[1].

This study aimed to determine the factors influencing morbidity and mortality in patients hospitalized due to COPD exacerbation by analyzing the data of six-year follow-up.

Material and Method

This research was designed as a retrospective cohort study and was approved by Cumhuriyet University Faculty of Medicine Local Ethics Committee.

The study included 178 out of 209 patients who admitted to our institution and were hospitalized in 2002 with diagnosis of COPD exacerbation. The patients who died during the hospitalization in 2002 and those who were out of reach in 2008 were excluded.

The initial demographic and anthropometric data, smoking history, asbestos and biomass exposure, comorbidities, the drugs and other treatments the patients used, laboratory parameters, arterial blood gases, pulmonary function tests were reached and noted from patients' files. If the records did not include the date of death, the patients or their families were reached by telephone. For those who could not be reached, local registry of population was searched.

For the statistical analyses, SPSS 14.0 (Statistical Package for Social Sciences, USA) program was utilized. The means of independent groups were compared with Student's t-test. Nominal variables were compared with chi square test or Fisher's exact test when necessary. Survival analysis was made. The data on tables were presented as mean ± standard deviation. A p value <0.05 was considered as significant. Confidence interval was defined as 95%.

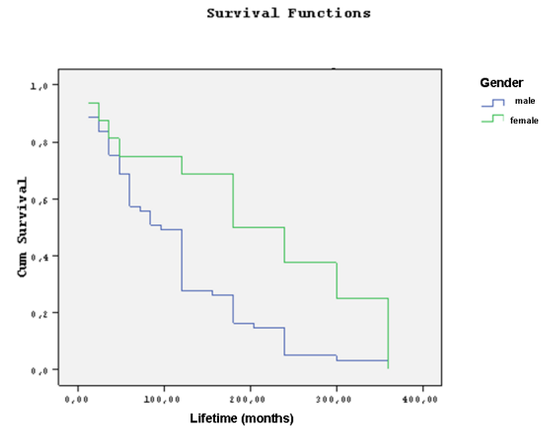
Results

The enrolled patients were classified as Group I (those who were alive by 2008, n: 64) and Group II (those who were dead by 2008, n: 114). The mean age and body mass index were not significantly different between two groups. However, the prevalence of women was higher in the first group compared to the second (Table 1).

Table 1. Basic characteristics of the patient groups.

		Group I (n: 64)	Group II (n: 114)	p
Age (year)		63.17±8.72	66.32±8.68	p=0.101
Body mass index		26.68±5.18	25.43 ±5.25	p=0.248
Sex	male	36 (56.3%)	83 (72.8%)	p=0.024
	female	28 (43.8%)	31 (27.2%)	

In the Group II, the duration between the time of diagnosis and the time of death was calculated. The average lifetime with a diagnosis of COPD was 111.9±11.1 months for men and 206.5±32.2 months for women. Median survival time was 96 months in men and 180 months in women with COPD. These results showed that there was an obvious difference in prognosis between male and female patients (p=0.003) (Figure 1).



In terms of smoking status, smoking burden (in pack-years), and the presence of major comorbidities (namely coronary artery disease, congestive heart failure, hypertension and diabetes mellitus), there was no difference between two groups (Table 2). The frequency of the patients with biomass exposure and the mean duration of exposure did not differ significantly between the groups. However, as for the asbestos exposure, the prevalence of the exposed patients was higher in the surviving group (p=0.029). There was again no difference with regard to the duration of exposure (Table 2).

There were no significant differences between two groups in terms of the use of major drug classes prescribed for COPD (Table 3).

The basal hemoglobin, hematocrite, white blood cell count, platelet count, erhythrocyte sedimentation rate and C-reactive protein (CRP) levels did not differ significantly between the study groups (Table 4). Similarly, no significant difference was observed in terms of biochemical parameters that were measured (Table 5). Arterial blood gas analysis, as well, showed no difference between the groups (Table 6).

When the pulmonary function parameters were compared, it was found that the average basal forced expiratory volume in 1 second (as percentage of predicted) was lower in the deceased patients (p=0.038). The other parameters (namely, forced expi-

Table 2. Smoking and environmental exposure status, and comorbidities of the patients.

	Group I (n: 64)	Group II (n: 114)	p
Smoking burden (pack-years)	37.77±28.94	46.85±23.35	p=0.107
Number of current smokers	31	62	p=0.329
Duration of asbestos exposure (years)	33.55±17.57	41.00±17.16	p=0.376
Number of cases exposed to asbestos	24	29	p= 0.029
Duration of biomass exposure (years)	31.25±11.25	37.52±17.95	p=0.400
Number of cases exposed to biomass	26	47	p=0.733
Number of patients with hypertension	22	34	p=0.733
Number of patients with coronary artery disease	5	12	p=0.647
Number of patients with diabetes mellitus	5	18	p=0.167
Number of patients with congestive heart failure	12	29	p=0.387

Table 3. The frequency of the use of several drug groups by the patients.

Groups	Beta-mimetics	Anticholiner-gics	Theophylline	Inhaled corticosteroids
Group I (survivors)	58 (90.6%)	56 (87.5%)	54 (84.4%)	25 (39.1%)
Group II (deceased)	97 (85.1%)	103 (90.4%)	102 (89.5%)	50 (43.9%)
	p=0.233	p=0.499	p=0.229	p=0.348

Table 4. Comparison of some hematologic parameters between the groups.

	n	Group I (n: 64)	n	Group II (n: 114)	p
Hemoglobin (g/dl)	60	15.46±1.79	112	14.90±2.52	p=0.107
Hematocrite (%)	60	47.50±5.44	112	46.63±8.26	p=0.386
White blood cells (/mm3)	59	12500±5300	112	13600±9900	p=0.348
Platelets (/mm3)(×103)	58	273.98±99.34	106	263.16±117.52	p=0.553
Erythrocyte sedimentation rate (mm/h)	56	26.25±29.40	102	22.80±26.8	p=0.457
CRP	35	93.62±93.48	71	83.04±93.49	p=0.585

Table 5. Comparison of some biochemical parameters between the groups.

	n	Group I (n: 64)	n	Group II (n: 114)	p
Glucose (mg/dl)	60	144.75±74.64	111	128.31±52.62	p=0.133
BUN (mg/dl)	60	24.15±15.42	112	25.25±13.66	p=0.628
Creatinin (mg/dl)	60	1.30±0.38	112	1.32±0.38	p=0.766
ALT (IU/l)	59	28.38±44.80	111	41.81±146.86	p=0.494
AST (IU/l)	58	29.24±37.90	111	42.09±139.73	p=0.493
LDH (IU/l)	57	404.78±146.50	107	437.17±212.67	p=0.306
Sodium (mmol/l)	58	139.50±4.46	106	137.83±5.07	p=0.052
Potassium (mmol/l)	57	4.35±0.74	107	4.35±0.75	p=0.974
Calcium(mg/dl)	57	8.60±0.61	104	8.45±0.72	p=0.213
Total protein (g/dl)	39	6.32±0.82	77	6.26±0.72	p=0.661
Albumin (g/dl)	40	3.59±0.50	77	3.41±0.46	p=0.059

ALT: alanine transferase, AST: aspartate transferase, BUN: blood urea nitrogen, LDH: lactate dehydrogenase.

ratory volume in 1 second [FEV1] in liters, forced vital capacity [FVC] in liters and as percentage of predicted, the ratio of FEV1 to FVC, and forced mid-expiratory flow in liters and as percentage of predicted) showed no significant difference between the groups (Table 7).

The patients in two groups did not differ significantly in the rate of the use of LTOT, non-invasive mechanical ventilation or nebulisator (Table 8). However, there was a significant difference between the groups considering the duration of LTOT use. The mean duration was 6.15±0.89 years in Group I and 1.30±0.76 years in Group II (p<0.001).

Discussion

COPD is a respiratory disease with a progressive nature that leads to substantial morbidity and mortality rates. The disease usually manifests itself later in life [3]. The gender ratio of the patients was reported to be 3:1 to 2:1 in favor of males [4]. Similarly, the average age in our series was 65.19± 8.80 years and two thirds of our patients were male.

Table 6. Comparison of arterial blood gas measurements between the groups.

	n	Group I (n: 64)	n	Group II (n: 114)	p
pH	44	7.42±0.06	95	7.41±0.07	p=0.137
PO2 (mmHg)	44	60.11±22.96	94	55.78±19.43	p=0.085
PCO2 (mmHg)	44	42.00±11.57	95	45.87±15.13	p=0.137
HCO3 (mEq/l)	44	27.36±6.41	95	28.87±6.64	p=0.211
SO2(%)	44	86.71±8.25	94	84.48±10.99	p=0.227
BE	42	3.40±5.45	93	4.05±5.02	p=0.500

BE: base excess, PO2: partial oxygen pressure, PCO2: partial carbon dioxide pressure, HCO3: bicarbonate, SO2: oxygen saturation

Table 7. Comparison of basal pulmonary function test parameters between the study groups.

	n	Group I (n: 64)	n	Group II (n: 114)	p
FEV1 (l)	29	1.07±0.39	54	1.02±0.39	p=0.527
FEV1 (%)	29	45.62±16.51	54	38.53±13.52	p=0.038
FVC (l)	29	1.91±0.66	54	1.88±0.55	p=0.860
FVC (%)	29	64.37±18.20	54	57.51±15.32	p=0.079
FEV1/FVC (%)	29	56.48±11.63	54	54.24±14.12	p=0.467
FEF25-75 (l/sn)	28	0.68±0.34	54	0.63±0.52	p=0.879
FEF25-75 (%)	28	21.96±11.72	54	21.35±11.23	p=0.870

FEF25-75: forced mid-expiratory flow, FEV1: forced expiratory volume in 1 second, FVC: forced vital capacity.

Table 8. The distribution of patients giving precise information on the use of long term oxygen treatment, non-invasive mechanical ventilation and nebulisator at home.

	Group I (n: 64)	Group II (n: 114)	p
LTOT users	27/52	60/91	0.099
LTOT non-users	25/52	31/91	
BiPAP users	1/52	3/90	0.990
BiPAP non-users	51/52	87/90	
Nebulisator users	10/52	22/90	0.510
Nebulisator non-users	42/52	68/90	

BiPAP: bi-level positive airway pressure, LTOT: long-term oxygen treatment.

Although the death rate due to COPD seems to be increasing among women, overall mortality remained higher in male patients [1]. Our study found a significantly higher mortality rate among men compared to women. This difference could be attributed to increased smoking rates and occupational exposure to noxious dust and particles in men.

Active smoking is associated with development of COPD and increased frequency of exacerbations [5]. Lung Health Study showed that current smokers lost more respiratory function capacity compared to ex-smokers [6]. Although statistically non-significant, the average smoking burden in deceased patients was higher than that in surviving patients. This difference could have an impact on clinical progression of the disease.

The systemic inflammation and oxidative stress in COPD result in weight loss and muscle wasting [7]. Several studies showed an association between lower body mass index and worse prognosis [8-10].; however, Karin et al. found that body mass index had no impact on mortality in COPD patients hospitalized due to exacerbation [11]. In this study, there was no difference in body mass index between surviving and deceased patients with COPD. However, intra-group analysis of Group II showed that those with a body mass index less than 20 had lived shorter.

The presence of comorbidities is accused to influence health outcomes in COPD and the most frequent comorbidities were reported to be hypertension, diabetes and ischemic heart disease [12]. Sin et al. found that comorbidities were independent risk factors for mortality in COPD exacerbations [13]. The prevalence of major comorbidities (hypertension, coronary artery disease, congestive heart failure, and diabetes mellitus) was not different between study groups.

Anemia was reported to be associated with dyspnea, low effort capacity, and shorter survival in COPD patients [14-16]. Cote et al. showed that 70% of COPD patients had anemia and 4% had polycythemia [14]. In our series, the average hemoglobin values were over anemic levels in both groups and were not statistically different to each other.

Leucocytosis in patients with COPD may be related to concomitant infections or steroid use. It was also reported to be correlated with decrease in pulmonary function [17,18]. Although statistically non-significant, the average leukocyte count in deceased patients was higher than that in surviving patients. Furthermore, intragroup analysis in Group II showed that the patients with a leukocyte count more than 10000/mm3 had shorter survival.

The increased CRP levels in patients with COPD are associated with the disease itself, the systemic inflammation in COPD, and cigarette smoking [19]. It was also found to be correlated with the severity of COPD and loss of respiratory function [20,21]. In contrast, Yasuda et al. found no association between CRP level and the severity of COPD [22]. Our study showed no difference in average CRP level between the study groups. It could be suggested that this result was related to high rate of smoking in both groups and CRP was measured during exacerbations.

COPD is one of the most important causes of chronic respiratory failure. Chronic hypercapnia and acidosis were demonstrated to be associated with worse prognosis in COPD by some studies [11,23,24]; however, Tessa et al. could not be find such association [25]. In our study, partial arterial oxygen pressure (PaO2) was lower and partial arterial carbon dioxide pressure (PaCO2) was higher in deceased patients. Furthermore, intra-group analysis in this group showed that the patients with PaO2<45 mmHg and PaCO2>55 mmHg had shorter survival. However, these results were not statistically significant and the authors believe it was due to low number of cases.

Long-term oxygen treatment (LTOT) was shown to provide longer survival in patients with COPD [2, 26]. Other researchers failed to demonstrate the beneficial effect of oxygen treatment on prognosis in mild-moderate hypoxemia(27,28). In our series, the duration of oxygen treatment was longer in surviving patients.

The retrospective design, the low number of cases and the inclusion of only one care center limit the conclusions of this study. In order to determine the prognostic factors in COPD thoroughly, prospective and multi-centered trials are needed.

Competing interests

The authors declare that they have no competing interests.

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